

will study the rainforests of Suriname. "And gums, tars, resins, insects, and leaves provide a wonderful source of new compounds that can be tested very efficiently and quickly. Even the tiniest compounds can now be picked up."

A number of plant-based drugs are already available, including the antitumor compound Taxol, made from the bark of the yew tree. But using plants as an important medicinal source can bring its own set of problems. In the Pacific Northwest of the United States, primary forests of mature yew trees were decimated because of heavy harvesting to make Taxol. Today, the compound is made semisynthetically, using only the tree's needles, according to Kingston. By helping local communities cultivate medicinal plants, the ICBG members hope to avoid the Taxol example.

While four of the teams will focus on plants, a team of entomologists from Cornell University plans to study some of the tens of thousands of insects found in the dry tropical forests of Costa Rica, according to Cornell entomologist and ICBG member Thomas Eisner. Insects have long been overlooked for their medicinal potential despite several recent discoveries such as active antiviral compounds found in fireflies. "Because insects are often tiny and easily threatened in their environments, they have had to create chemical defenses," says Eisner. "We think this could be a new kind of treasure." However, such rainforests are shrinking as a result of regional development, so there is an urgency to accelerate research and collaboration.

"Most natural compounds have not yet been discovered," says Eisner. "And many species are fast disappearing, which is a great shame because the best things on the market are all derived from nature."

Ethnobotanists believe desert plants may also produce promising medicinal compounds. Unable to move or escape, desert organisms have had to adapt, anatomically and chemically, to high heat, intense sun, and lack of water. In order to survive, they produce "many unusual chemicals to protect themselves," says ICBG member Barbara Timmermann, a phytochemist at the University of Arizona. These chemicals can then be studied for their therapeutic activity in human disease.

Timmermann's team will be working closely with native healers to carefully select plants from the hundreds of species that inhabit the hot deserts of Chile and the cold deserts of southern Argentina, especially Patagonia and Tierra del Fuego. Because of the preliminary nature of their work, Timmerman is reluctant to identify any particular plant that might have potential. Like her colleagues on other ICBGs, she fears that until toxicological studies prove a

plant harmless, sick people may gather its leaves and try to treat themselves.

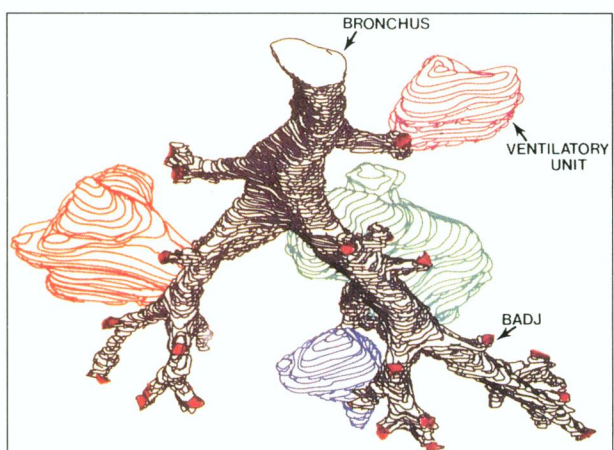
Silicon Lungs

Open to the environment, the lung's airways continuously take in the atmosphere and process the good and the bad through a branching maze of bronchi and alveolar air sacs. Just how—and how much—pollution affects human lungs has largely remained a mystery. One institution, the Center for Extrapolation Modeling at Duke University Medical Center, is making progress in understanding how human lungs interact with environmental toxins. Researchers at the center, formed in 1986 with the help of EPA and industry funding, are now able to demonstrate, for example, what a summertime's exposure to ozone and freeway gases in Los Angeles does to the lungs of a rat. The center's 10-member team of respiratory physiologists, cell biologists, engineers, and mathematicians is now calculating how equivalent doses of pollutants affect human lungs.

Using data on lung structure and organization from a variety of different types of pathologic analyses, the center is slowly and steadily deriving a computer-based, three-dimensional model of both animal and human lungs that can be used to help predict where different doses of a particular pollutant will cause damage. The task is extremely complicated given that only limited data are available from human studies, said the center's director, James D. Crapo. "We have to create a database to predict effects which are unknown or for which data cannot be accumulated," he said.

Currently, the EPA sets air quality standards based on human epidemiologic studies and on animal studies using the assumption that if a certain pollutant causes injury in animals, then it must also be harmful to humans. What isn't known, said Crapo, is what concentrations of common air pollutants cause injury in humans and exactly where that damage occurs. "Our goal is to find ways to predict where in the lungs different pollutants go, their dose at specific sites, and the types of damages they cause," he said.

The center's researchers are using the only data available to them—known effects of air pollution in studies of animal lungs. Then, using mathematical modeling, the researchers derive experimental correlations that can provide input for extrapolation from acute and chronic lung disease in ani-



Virtual reality. Computer-based models of rat lungs may help show where pollutants lodge in lungs of humans.

mals to humans, said Crapo.

It's an intricate process. Animal lungs behave differently from human lungs. The lungs of a rat have airways that are shaped like a pine tree because of their straight, monopodial branching system. But human lungs, with airways that have an irregular, dichotomous branching pattern, are more like an oak tree. Because of this, particles and gas that might be absorbed in one area in rat lungs would likely be processed in a different place in human lungs. Each species also has varying types of cells in different locations in their lungs.

To determine these differences and evaluate their significance, scientists at the center are conducting toxicology studies of cells of the alveolar regions and small airways of animals exposed to varying doses of different airborne pollutants. These data are gathered by techniques such as immunocytochemistry, *in situ* hybridization, electron microscopy, and magnetic resonance microscopy. Researchers at the center are also leading the field in gathering microdosimetry data, the calculation of pollution dose at specific cells in each of the different regions of the lungs using labeled gases and particles in combination with microscopy, autoradiography, or positron emission tomography. "In five years we'd like to have developed a computer system that simulates every aspect of the process of breathing based on all the data we've collected," said Crapo. "We could introduce different pollutants into the system and determine in real-time exactly where in the lungs they go."

Philip Bromberg, director of the University of North Carolina Center for Environmental Medicine and Lung Biology, says the Duke lung modeling program is as ambitious as it is unique. "With a structure as complicated as a lung, it is difficult to reconstruct a 3-D piece of even a small portion. This is not like a piece of bologna, where you can figure out what the

whole looks like from a slice." Bromberg said that when the model is further advanced, it will offer his center, and others, chances to collaborate. "We work to understand how human cells react to toxicity. That's an important piece of the picture of lung function we all are trying to reach."

Contaminants in Fish

From the icy waters of Boston Harbor to the warm waves of San Diego Bay, bottom-dwelling fish suffer liver damage caused by chemical contaminants, according to researchers at the National Oceanic and Atmospheric Administration.

But seafood lovers need not panic, because damaged specimens were captured primarily in urban waters where commercial fishing is prohibited, said Lyndal L. Johnson of NOAA's Northwest Fisheries Science Center in Seattle, Washington.

"This is not a situation where the general public needs to be really worried about the fish they buy in the supermarket," Johnson said, adding that most people don't eat fish livers anyway. "But I wouldn't go out and catch bottom fish in contaminated parts of Boston Harbor and eat them."

In a study of winter flounder collected from 22 sites along the Northeast Coast, Johnson found that liver damage was "significantly elevated" in fish from contaminated urban waters such as Boston Harbor, Massachusetts, and Raritan Bay, New York. Biological damage was attributed to polycyclic aromatic hydrocarbons (PAHs), DDT, and chlordanes. Yet, polychlorinated biphenyls (PCBs) were "not significant risk factors for any of the lesions observed," Johnson wrote in the December 1993 issue of *Environmental Science & Technology*. Oil street runoff and industrial processes add PAHs to urban waters. DDT, chlordanes, and other ecologically persistent pesticides remain in water despite bans and restrictions on their use.

Older fish are most likely to be affected by such contaminants, Johnson said. Female specimens captured during the spawning season seemed less vulnerable to contaminants, but Johnson cautioned that this finding has not yet been confirmed. (Spawning fish may have migrated to urban bays from less contaminated waters.)

A second NOAA study prepared by Johnson's colleague Mark S. Myers revealed that English sole, starry flounder, and white croaker captured from 27 sites along the West Coast, from Alaska to southern California, were also affected by chemical contaminants. Liver damage and cancers were prevalent in fish collected from urban waters surrounding Los Angeles, as well as Puget Sound, San Francisco Bay, and San

Diego Bay, Myers reported in the February 1994 issue of *EHP*. Lesions were linked to PAHs, DDT, and its derivatives, chlordanes, dieldrin (an insecticide), aromatic hydrocarbons, and PCBs. Like Johnson, Myers detected more liver damage in older fish. Yet, he reported that gender of fish was not a consistent risk factor.

Faced with conflicting information on PCBs, Johnson and Myers can only speculate that these contaminants may work with other chemicals to promote liver damage. "What we think might be happening is that the primary carcinogens, the ones that cause DNA damage or mutations, are the PAHs, while the PCBs are promoters," Johnson said. "Once DNA damage or mutagenic effects have occurred, PCBs may promote the growth of those damaged cells." Chlordane and aromatic hydrocarbons may also require further study. Johnson linked an abnormality known as "hydropic vacuolation" with exposure to PAHs and chlordane. But in previous research by M.J. Moore of the Woods Hole Oceanographic Institute, winter flounder exhibited no such response to these contaminants. Yet, Moore supports the NOAA findings and says his "exposure protocol" probably didn't reflect natural conditions. "I would not interpret negative results to confound the good statistical work" of the NOAA team, Moore said.

While researchers continue to investigate the biological effects of various contaminants, consumers should simply avoid eating fish livers, said Chester Zawacki of New York's Department of Environmental Conservation. "The liver is an organ that has been referred to jokingly as the oil filter of the body," he noted. Because pollutants accumulate in fatty tissues, heavily fattened fish such as striped bass are most vulnerable

to contamination. "Winter flounder, cod, and other low-fat fish generally show very little contamination of their edible tissues," Zawacki said.

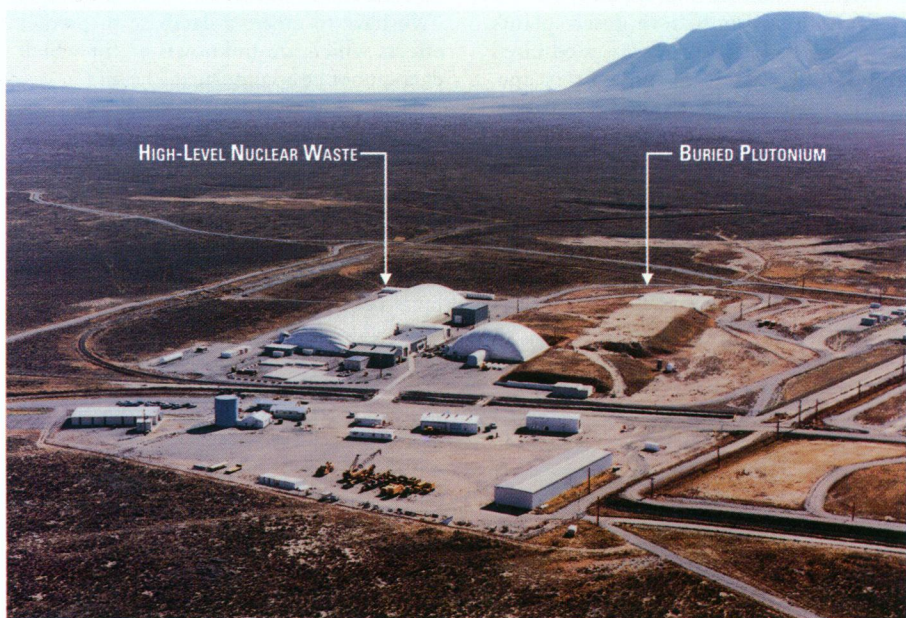
While the verdict may be out on the effects of eating contaminated fish, the Department of Health and Human Services has moved to err on the side of caution. On January 21, Secretary Donna Shalala announced new rules for seafood handling that will require seafood processors to prove that their seafood has not been exposed to unacceptable levels of water pollution such as bacterial contamination or toxins. The new system of controls, known as Hazard Analysis Critical Control Points, will take effect a year from the end of a 90-day public comment period.

Plutonium Problems

The Department of Energy's recent discovery of approximately 1900 pounds of plutonium in a dump at the Idaho National Engineering Laboratory (INEL) underscores concerns about the impact of nuclear facilities on surrounding communities.

In December 1993, the Department of Energy estimated that between 1320 and 1980 pounds of plutonium waste were sent to INEL from the Rocky Flats nuclear weapons plant near Denver, in addition to 807 pounds that DOE previously said had been shipped to Idaho. The wastes are buried in a landfill that sits atop a widely used aquifer.

Idaho officials do not yet know whether the additional wastes increase health risks to area residents, according to Terry Smith, spokesman for the state's INEL monitoring program, though no plutonium has been found in the aquifer, he said.



Striking plutonium. DOE recently discovered 1900 pounds of plutonium buried in a dump in Idaho.

DOE/Idaho